REMARKS

The Examiner is requested to note that the claims prior to this Amendment could be divided into the following groups:

(1) A method of obtaining isolated selected mRNA species or isolated selected cDNA species useful for diagnosing or identifying a disease or stage thereof - using mRNA isolated from cells of one or more eukaryotic organisms which are known to have said disease or a stage thereof - wherein the cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease (Claims 37, 40-43, 45-46 and 48-52);

(2) A method of preparing a gene transcript pattern probe kit using mRNA isolated from cells of one or more eukaryotic organisms which are known to have a disease or a stage thereof - wherein the cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease (Claims 56, 39 and 47);

(3) A method of preparing a standard gene transcript pattern characteristic of a disease or stage thereof of a eukaryotic organism using mRNA isolated from cells of one or more eukaryotic organisms known to have said disease or a stage thereof - wherein the cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease (Claims 57 and 60-65);

(4) A method of preparing a test gene transcript pattern for a disease or stage thereof using isolated mRNA from cells of a test eukaryotic organism - wherein the cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease (Claims 58 and 66-71);

(5) A method of diagnosing or identifying a disease or stage thereof in a test eukaryotic organism using mRNA isolated from cells of a test eukaryotic organism - wherein the cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease (Claims 59, 72-77);

(6) A method of obtaining isolated selected mRNA species or isolated selected cDNA species useful for diagnosing or identifying Alzheimer's disease or stage thereof in a human using mRNA isolated from human cells - wherein the cells are obtained from a part of said humans distant to the area of said disease (Claim 78-86);

(7) A method of preparing a gene transcript pattern probe kit using mRNA isolated from cells of one or more humans which are known to have Alzheimer's disease or a stage thereof - wherein the cells are obtained from a part of said humans distant to the area of said disease (Claims 87-89);

(8) A method of preparing a standard gene transcript pattern characteristic of Alzheimer's disease or stage thereof using mRNA isolated from cells of one or more humans known to have said disease or a stage thereof, wherein the cells are obtained from a part of said humans distant to the area of said disease (Claims 90 and 93-94);

(9) A method of preparing a test gene transcript pattern for Alzheimer's disease or stage thereof using mRNA isolated from cells of a test human - wherein the cells are obtained from a part of said human distant to the area of said disease (Claims 91 and 93-94); and

(10) A method of diagnosing or identifying Alzheimer's disease or stage thereof in a test human using mRNA isolated from cells of a test human - wherein the cells are obtained from a part of said

human distant to the area of said disease Claims 92 and 93-94).

Solely in order to advance prosecution, Applicants hereby cancel Claims 37-77 (groups (1)-(5) above) without prejudice or disclaimer to purse the subject matter thereof in a continuing application. This present application is now directed to Claims 78-94 (groups (6)-(10) above). Further, the independent claims (Claims 78, 87, 90, 91 and 92) have been amended to include the recitation of Claims 86 and 94 therein, thereby resulting in the cancellation of Claims 85-86 and 93-94.

In paragraph 3, on page 2 of the Office Action, the Examiner maintains the rejection of Claims 37, 39-43, 45-52 and 56-94 under 35 U.S.C. § 112, first paragraph.

The rejection is being maintained for the following four (4) reasons:

(1) The Examiner acknowledges that the specification is enabling for methods for obtaining isolated selected mRNA species useful for diagnosing or identifying a disease or condition where the mRNA is isolated from cells that are obtained from a part of the organism distant to the area of disease. However, it is the Examiner's position that the specification does not provide enablement for the full scope of methods involving cells that have not contacted the area of disease.

Specifically, the Examiner states, at page 6 of the Office Action, that the specification does not provide guidance on how to identify cells in a sample which have not come into contact with the area of disease, except for the case where the area of disease is the brain, as in Alzheimer's disease.

As the claims have limited to Alzheimer's Disease, and the objected to language ("a part of the organism distant to the area of disease") has been removed form the pending claims, Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

(2) The specification is not enabling for methods in which the disease is Alzheimer's disease (Claims 78-94 - Groups (6)-(10), above).

The Examiner has reviewed the Declaration evidence of record and does not find such convincing as to claims limited to Alzheimer's disease.

Specifically, the Examiner contends that no statistical analysis is given on the differentially expressed genes or evidence that the differential expression pattern is particular to Alzheimer's disease because there is no other "diseased control" present, i.e., it is the Examiner's position that it is not possible to determine whether diagnosis would be specific to Alzheimer's disease or merely to a "stressed" state (see pages 3-4 of the Office Action).

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Applicants submit herewith a "Second Declaration under Rule 132" addressing the Examiner's concerns. Specifically, the

Second Declaration provides, *inter alia*, a statistical analysis of the differentially expressed genes of (i) subjects afflicted with Alzheimer's Disease (and no breast cancer); (ii) subjects afflicted with breast cancer (and no Alzheimer's disease); and (iii) healthy subjects (with neither Alzheimer's disease nor breast cancer), as well as evidence that the differential expression pattern is particular to Alzheimer's disease vs. "diseased control" (the breast cancer subjects) and "healthy control" (normal subjects). The analysis of the differentially expressed genes clearly shows a statistically significant level of expression of particular genes in the diseased samples vs. the non-diseased samples, and that one can use the method of the present invention to diagnose Alzheimer's disease. The analyses also show that the differentially expressed genes are concerned with so-called "house keeping functions" in the cell, and are not classically considered to be "stress-related" genes.

(3) The Examiner contends that the specification is not enabling with respect to all diseases or conditions in all eukaryotes, i.e., a representative number of examples has not been provided with respect to a variety eukaryotes and diseases.

In this regard, the Examiner has also reviewed the Declaration evidence of record and does not find such convincing as to claims limited to breast cancer.

Specifically, the Examiner contends that there is no statistical validation to confirm that two genes are differentially expressed between the diseased and control

patients, nor does the experiment validate the ability of the method to diagnose breast cancer versus a different disease.

Furthermore, the Examiner states that no data is given in the Declaration as to which genes are being differentially expressed or what levels. Thus, the Examiner concludes that it is impossible to determine from the data in the Declaration if, for example, the same genes are being differentially expressed in Alzheimer's samples and breast cancer samples.

In addition, the Examiner states that the Declaration does not address how to determine whether or not the cells being tested have come into contact with the area of disease in the case of breast cancer, and it is unclear how to determine from the blood sample used, which cells have come into contact with the tumor.

As the claims have limited to Alzheimer's disease, Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot. Nonetheless, Applicants respectfully submit that the evidence presented in the Second Declaration clearly validates the ability of the method to diagnose breast cancer versus a different disease (Alzheimer's disease) with using blood sample obtained from an area (the arm) distant to the disease site (the breast).

(4) The Examiner contends that the claims broadly encompass detection of a disease or condition using a variety of body fluids or body parts, and yet the examples only provide evidence as to blood.

Solely, in order to advance prosecution, the body fluids are hereby limited to human blood. Thus, Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot. Applicants make this amendment without prejudice or disclaimer to pursue broader subject matter in a continuing application.

Accordingly, Applicants respectfully submit that the claims are enabled by the specification, and thus request withdrawal of the Examiner's rejection.

In view of the amendments to the claims and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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